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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CROW, ROBERT THOMAS	
ART UNIT	PAPER NUMBER
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/750,315	BERLIN ET AL.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-23 and 36-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-23 and 36-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 31 October 2006 has been entered.

Status of the Claims

2. This action is in response to papers filed 31 October 2006 in which claims 18, 21, and 23 were amended, no claims were canceled, and new claims 36-40 were added. All of the amendments have been thoroughly reviewed and entered.

The previous rejections under 35 U.S.C. 112, second paragraph, are withdrawn in view of the amendments.

The previous rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) not reiterated below are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections necessitated by the amendments.

Claims 18-23 and 36-40 are under prosecution.

Claim Rejections - 35 USC § 112 First Paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 23 and 40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 23 and 40 each recite "a mesh inside the inlet channel or the outlet channel" in lines 1-2 of each of the claims. However, the specification does not teach a mesh inside the inlet channel. Paragraph 19 on page 4 of the specification teaches nucleotides flowing through the chamber into the channel, which can include a mesh. Because the nucleotides have already flowed through the chamber, the mesh is clearly in the outlet channel. Paragraph 82 on page 20 of the specification teaches a mesh in the channel, but does not specifically teach the mesh in either an inlet or outlet channel. Paragraph 99 on page 26 of the specification also teaches a mesh in the channel, but does not specifically teach the mesh in either an inlet or outlet channel. Thus, while paragraph 19 supports a mesh in the outlet channel, the specification does not provide support for a mesh in the inlet channel. Thus, the inclusion of a mesh specifically in the inlet channel constitutes new matter.

Claim Rejections - 35 USC § 112 Second Paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 23 and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 23 and 40 are each indefinite in following:

A. The recitation "a mesh inside the inlet channel or the outlet channel comprising" in lines 1-2 of each of the claims. It is unclear if the claim requires the mesh to be made of the recited metals or if

the claim required the channels themselves to be made of the recited metals. It is suggested the claims be amended to indicate which structural component comprises the recited metals.

B. The recitation "or aluminum SERS active nanoparticles" at the end of each of the claims. The placement of the word "or" makes it unclear if all of the metals listed are required to be SERS active metal nanoparticles or if the SERS active metal nanoparticles are only made of aluminum. It is suggested the claims be amended to indicate which metals are also required to be SERS active metal nanoparticles.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 18-23 and 36-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shipwash (U.S. Patent Application Publication No. US 2002/0058273 A1, published 16 May 2002) in view of Natan (U.S. Patent Application Publication No. US 2002/0142480 A1, published 3 October 2002).

Regarding claim 18, Shipwash teaches an apparatus. In a single exemplary embodiment, Shipwash teaches a reaction chamber containing a single template nucleic acid molecule attached to an immobilization surface; namely, a bead (paragraph 0043). The apparatus of Shipwash further comprises an inlet channel in fluid communication with the reaction chamber; namely, Figure 22, wherein the inlet channel comprises the channel having the digestion chamber (paragraphs 0482-0484. Shipwash also teaches the apparatus comprises an outlet channel in fluid communication with the reaction chamber; namely, Figure 22, wherein the outlet channel is end of one of the reaction channels (paragraphs 0482-0484).

Shipwash also teaches a first Raman detection unit operably coupled to the inlet channel; namely, an optical detector is integrated onto the inlet digestion chamber (paragraph 0484), wherein Raman Spectroscopy is used (paragraph 0174), as well as a second Raman detection unit operably coupled to the outlet channel of Figure 22, wherein the detector is a Raman spectrophotometer and Raman Spectroscopy is used; paragraphs 0224 and 0174).

Shipwash does not teach the Raman detection units configured for surface enhanced Raman spectroscopy.

However, Natan teaches the Raman detection units configured for surface enhanced Raman spectroscopy (paragraph 0042) with the added advantage that surface enhanced Raman spectroscopy allows detection of molecules attached to the surface of a single metal nanoparticle in multiplexed assay formats (paragraph 0006), thereby increasing the sensitivity of the detection and increasing the number of different molecules detectable in a single assay.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the apparatus comprising two Raman detection units of Shipwash with detectors of surface enhanced Raman spectroscopy as taught by Natan with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in allowing detection of molecules attached to the surface

of a single metal nanoparticle in multiplexed assay formats, thereby increasing the sensitivity of the detection and increasing the number of different molecules detectable in a single assay, as explicitly taught by Natan (paragraph 0006).

Regarding claim 19, the apparatus of claim 18 is discussed above. Shipwash also teaches each Raman detection unit is capable of detecting at least one nucleotide at the single molecule level (paragraph 0168).

Regarding claim 20, the apparatus of claim 18 is discussed above. Shipwash also teaches the concentrations of nucleotides are measured by Raman spectroscopy as they flow through the inlet channel and the outlet channel; namely, the system detects concentration (paragraph 0170) and uses Raman spectroscopy (paragraph 0174).

In addition, the courts have held that "while features of an apparatus may be recited either structurally or functionally, claims directed to an apparatus must be distinguished from the prior art in terms of structure rather than function." *In re Schreiber*, 128 F.3d 1473, 1477-78, 44 USPQ2d 1429, 1431-32 (Fed. Cir. 1997). In addition, "[A]pparatus claims cover what a device *is*, not what a device *does*." *Hewlett-Packard Co. v. Bausch &Lomb Inc.*, 909 F.2d 1464, 1469, 15 USPQ2d 1525, 1528 (Fed. Cir. 1990) (emphasis in original). Therefore, the various uses recited in claim 20 (e.g., measuring concentration of nucleotides) fail to define additional structural elements to the device of claim 18. Because Shipwash in view of Natan teaches the structural elements of claim 18, claim 20 is obvious over the prior art.

Regarding claim 21, the apparatus of claim 18 is discussed above. Shipwash teaches nucleic acids are on metal particles in channels (paragraph 0043), which is interpreted as being in the inlet and outlet channels. Shipwash does not explicitly teach surface enhanced Raman spectroscopy active particles.

However, Natan teaches surface enhanced Raman spectroscopy active particles; namely, SERS active composite nanoparticles, which have the added advantages of being stabilized against decomposition of the analyte in solvent and air, chemically inert, and easily centrifuged and redispersed without loss of SERS activity (paragraphs 0007-0009).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the apparatus comprising two Raman detection units of Shipwash with the surface enhanced Raman spectroscopy active particles as taught by Natan with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in particles that are stabilized against decomposition of the analyte in solvent and air, chemically inert, and easily centrifuged and redispersed without loss of SERS activity as explicitly taught by Natan (paragraph 0007-0009).

Regarding claim 22, the apparatus of claim 18 is discussed above. Shipwash also teaches the inlet channel and outlet channel diameter is between about 100 and about 200 micrometers in diameter (paragraph 0210).

Regarding claim 23, the apparatus of claim 18 is discussed above. While Shipwash also teaches the apparatus further comprises a mesh in the form of filter and grids that retain nanoparticles in the channels of the apparatus (paragraphs 0167 and 0270), Shipwash is silent with respect to the materials used for the mesh.

However, Natan teaches SERS sandwich nanoparticles (i.e., SSNs; paragraph 0020 and Figure 1) made of gold (paragraph 0047) wherein the SSNs interlock to form a mesh and having the added advantage that the mesh allows the overall shape of the SSNs, and thus the mesh, to be chosen (paragraph 0031). Natan also teaches that the use of gold allows ready chemical enhancement of the SERS nanoparticles (paragraph 0029).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the apparatus comprising the mesh having retained nanoparticles of Shipwash with meshed gold nanoparticles as taught by Natan with a reasonable expectation of success. The retention of the meshed nanoparticles of Natan on the mesh of Shipwash would result in a mesh inside the channel comprising surface enhanced Raman spectroscopy active gold nanoparticles. The ordinary artisan would have been motivated to make such a modification because said

modification would have resulted in a mesh with a controlled overall shape as well as nanoparticles that are readily chemically enhanced as explicitly taught by Natan (paragraphs 0031 and 0029).

Regarding claim 36, Shipwash teaches an apparatus. In a single exemplary embodiment, Shipwash teaches a reaction chamber containing a single template nucleic acid molecule attached to an immobilization surface; namely, a bead (paragraph 0043). The apparatus of Shipwash further comprises an inlet channel in fluid communication with the reaction chamber; namely, Figure 22, wherein the inlet channel comprises the channel having the digestion chamber; paragraphs 0482-0484. Shipwash also teaches the apparatus comprises an outlet channel in fluid communication with the reaction chamber; namely, Figure 22, wherein the outlet channel is end of one of the reaction channels (paragraphs 0482-0484).

Shipwash also teaches a first Raman detection unit operably coupled to the inlet channel; namely, an optical detector is integrated onto the inlet digestion chamber (paragraph 0484), wherein Raman Spectroscopy is used (paragraph 0174), as well as a second Raman detection unit operably coupled to the outlet channel of Figure 22, wherein the detector is a Raman spectrophotometer and Raman Spectroscopy is used; paragraphs 0224 and 0174). Shipwash further teaches nucleic acids are on metal particles in channels (paragraph 0043), which is interpreted as being in the inlet and outlet channels.

Shipwash does not teach Raman detection units configured for surface enhanced Raman spectroscopy, nor does Shipwash does not explicitly teach surface enhanced Raman spectroscopy active particles.

However, Natan teaches the detectors configured to perform surface enhanced Raman spectroscopy (paragraph 0042) with the added advantage that surface enhanced Raman spectroscopy allows detection of molecules attached to the surface of a single metal nanoparticle in multiplexed assay formats (paragraph 0006) thereby increasing the sensitivity of the detection and increasing the number of different molecules detectable in a single assay. Natan also teaches surface enhanced Raman spectroscopy active particles; namely, SERS active composite nanoparticles, which have the added advantages of being

stabilized against decomposition of the analyte in solvent and air, chemically inert, and easily centrifuged and redispersed without loss of SERS activity (paragraphs 0007-0009).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the apparatus comprising two Raman detection units and nanoparticles of Shipwash with detectors of surface enhanced Raman spectroscopy and the surface enhanced Raman spectroscopy active particles as taught by Natan with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in allowing detection of molecules attached to the surface of a single metal nanoparticle in multiplexed assay formats thereby increasing the sensitivity of the detection and increasing the number of different molecules detectable in a single assay, as well as providing particles that are stabilized against decomposition of the analyte in solvent and air, chemically inert, and easily centrifuged and redispersed without loss of SERS activity as explicitly taught by Natan (paragraphs 0006-0009).

Regarding claim 37, the apparatus of claim 136 is discussed above. Shipwash also teaches each Raman detection unit is capable of detecting at least one nucleotide at the single molecule level (paragraph 0168).

Regarding claim 38, the apparatus of claim 36 is discussed above. Shipwash also teaches the concentrations of nucleotides are measured by Raman spectroscopy as they flow through the inlet channel and the outlet channel; namely, the system detects concentration (paragraph 0170) and uses Raman spectroscopy (paragraph 0174).

In addition, as noted above, the courts have held that while features of an apparatus may be recited either structurally or functionally, claims directed to an apparatus must be distinguished from the prior art in terms of structure rather than function. Therefore, the various uses recited in claim 38 (e.g., measuring concentration of nucleotides) fail to define additional structural elements to the device of

claim 36. Because Shipwash in view of Natan teaches the structural elements of claim 36, claim 38 is obvious over the prior art.

Regarding claim 39, the apparatus of claim 36 is discussed above. Shipwash also teaches the inlet channel and outlet channel diameter is between about 100 and about 200 micrometers in diameter (paragraph 0210).

Regarding claim 40, the apparatus of claim 36 is discussed above. While Shipwash also teaches the apparatus further comprises a mesh in the form of filter and grids that retain nanoparticles in the channels of the apparatus (paragraphs 0167 and 0270), Shipwash is silent with respect to the materials used for the mesh.

However, Natan teaches SERS sandwich nanoparticles (i.e., SSNs; paragraph 0020 and Figure 1) made of gold (paragraph 0047) wherein the SSNs interlock to form a mesh and having the added advantage that the mesh allows the overall shape of the SSNs, and thus the mesh, to be chosen (paragraph 0031). Natan also teaches that the use of gold allows ready chemical enhancement of the SERS nanoparticles (paragraph 0029).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the apparatus comprising the mesh having retained nanoparticles of Shipwash with meshed gold nanoparticles as taught by Natan with a reasonable expectation of success. The retention of the meshed nanoparticles of Natan on the mesh of Shipwash would result in a mesh inside the channel comprising surface enhanced Raman spectroscopy active gold nanoparticles. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a mesh with a controlled overall shape as well as nanoparticles that are readily chemically enhanced as explicitly taught by Natan (paragraphs 0031 and 0029).

Response to Arguments

11. Applicant's arguments filed 31 October 2006 with respect to the rejection of the claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571) 272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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SUPERVISORY PATENT EXAMINER

Robert T. Crow
Examiner
Art Unit 1634